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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,064	10/05/2005	Oliver Schadt	MERCK-3067	6539

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MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

EXAMINER	
JARRELL, NOBLE E	

ART UNIT	PAPER NUMBER
1624	

NOTIFICATION DATE	DELIVERY MODE
09/03/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@mwzb.com

Office Action Summary	Application No.	Applicant(s)	
	10/552,064	SCHADT ET AL.	
	Examiner	Art Unit	
	NOBLE JARRELL	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,15-24 and 27-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,15,16,19,21 and 27-29* is/are rejected.

7)☒ Claim(s) *17,18,20,22 and 24* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/31/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Current Status of 10/552064

1. In the current claim set, claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 27, 28, and 29 are pending. These claims are being examined on the merits.

2. The information disclosure statement filed 3/31/2009 is acknowledged and ahs been considered.

Information Disclosure Statement

3. The information disclosure statement filed 21 March 2009 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. It has been placed in the application file, but the information referred to therein has not been considered. The relevance of reference C13 is difficult to determine because only the first page of the reference has been provided. The first page only describes a broad genus of compounds that could encompass a compound embraced by formula I.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 11-13, 16, and newly added claim 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *in vitro* binding of compounds of formula I to 5-HT_{2A} receptors, does not reasonably provide enablement for treatment of diseases that can be related to binding to a 5-HT receptor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed.

Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Consideration of the relevant factors sufficient to establish a *prima facie* case for lack of enablement is set forth herein below:

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to binding compounds composed of a 1-phenyl-pyrazole or 1-(2-pyridyl)-pyrazole core structure to a serotonin receptor. Thus, the claims taken together with the specification imply that diseases can be treated with compounds of formula I.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

Wood et al. (*Expert Opinion in Investigational Drugs*, **2002**, *11(4)*, 457-67) teach that therapeutic efficacy remains to be seen for modulation of serotonin receptors. Wood et al. imply that future research is needed to determine if the therapeutic efficacy is a viable target (page 463, last paragraph of section 7).

Crow (*Expert Opinion in Investigational Drugs*, **1997**, *6(4)*, 427-36, previously cited) teaches that eating disorders cannot be treated by drugs alone ("Conclusion" section, pages 433-34). This teaching implies that future research is needed to determine of serotonin modulators will show a significant improvement over already existing compounds.

(5) The relative skill of those in the art:

Those of relative skill in the art are those with level of skill of the authors of the references cited to support the examiner's position. The relative skill of those in this art is MD's, PhD's, or those with advanced degrees and the requisite experience in treatment of diseases related to compounds that bind to serotonin receptors.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for *in vitro* binding of compounds of formula I to 5-HT_{2A} receptors.

However, the specification does not provide guidance for treatment of diseases that can be related to binding to a 5-HT receptor.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to claims 11-13, 16, and newly added claim 29 and the high unpredictability in the art as evidenced therein, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

This rejection is maintained because Wood et al. and Crow show that future research in the field of serotonergic modulation.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-13, 15-16, 19, 21, 23, 27, newly added claim 28, and newly added claim 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claim 11, it is unclear

what specific disease is intended to be treated. The claim is drawn to only treatment of disease which can be influenced by binding of a compound of formula I to a serotonin receptor (a functional limitation). In claims 1-13, 15-16, 19, 21, 23, and 27, it is unclear what the variable "Het" stands for. The definition provided in claim 1 encompasses any ring with a heteroatom or any organic substituent that contains a heteroatom. What specific "neurological disorder" is referred to in clam 16 ("Neurodegenerative Diseases", http://www.nlm.nih.gov/cgi/mesh/2008/MB_cgi, accessed December 8, 2008, cited previously)? This rejection is maintained because applicants still have not specified which neurological disorder they intend to treat. Variable "Het" is still unclear because the definition encompasses any organic moiety with at least one heteroatom.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 1, 2, 3, 4, 7, 10, 15, 19, 20, 21, 23, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xiang et al. (WO 98/31227, published 23 July 1998, cited in 3/31/2009 IDS).

Determining the scope and contents of the prior art

Xiang et al. teach a compound in which a pyrazole ring is modified at following positions: at the 1-position by a *p*-(3-aminophenyl)-phenyl group; at the 4-position by CO_2Et; and at the 5-position by an O-ethylene-1-morpholino group. This compound is listed on page 18, line 4 of the reference. Compositions comprising this compound are taught on page 19 in example 65. Administration of the composition is taught on page 19 in example 64. Xiang et al. teach that a hydrogen atom substituent (for variable R_5 of WO 98/31227) is equivalent to a C_{1-8}alkyl group (page 3, line 25).

Ascertaining the differences between the prior art and the claims at issue

In the prior art, variable R^1 is (*m* or 3)-aminophenyl. In the instant application, variable R^1 is (*p* or 4)-dimethylaminophenyl.

Resolving the level of ordinary skill in the pertinent art

Those of relative skill in the art are those with level of skill of the authors of the references cited to support the examiner's position. The relative skill of those in this art is MD's, PhD's, or those with advanced degrees and the requisite experience in preparation of compounds of the formula I.

Considering objective evidence present in the application indicating obviousness or nonobviousness

In re Norris (84 USPQ 458) teaches "Counsel for applicant in their brief acknowledge that the record herein does not establish new and useful compound defined by the rejected claim possesses one or more specifically identified properties to be recognized as unobvious or unexpected, as measured by every conceivable standard. Since the product claimed herein admittedly possesses no unexpected characteristics or properties, in view of what has hereinbefore been said, it is not patentable."

Xiang et al. teach that a hydrogen atom substituent (for variable R_5 of WO 98/31227) is equivalent to a C_{1-8}alkyl group (page 3, line 25).

In a comparison of the prior art and the compound prepared and administered by Xiang et al., two differences exist: the position of the amino group on the phenyl ring and the presence of a

dimethylamino (*para* in 10/552064) and NH_2 (*meta* in WO 98/31227). Motivation to prepare the compound exists because Xiang et al. are using the compound a modulator of a cannabinoid receptor (the compound described is a final product, not an intermediate product).

Conclusion

11. Claims 17, 18, 20, 22, and 24 are objected to as being dependent upon a rejected base claim, but are seen to be free of the prior art. The compounds, which contain specific definitions (piperazinyl, pyrrolidinyl, or dialkylamino groups) for variable "Het" at present appear allowable and will be considered for allowance if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Xiang et al. teach a compound in which a pyrazole ring is modified at following positions: at the 1-position by a *p*-(3-aminophenyl)-phenyl group; at the 4-position by CO_2Et; and at the 5-position by an O-ethylene-1-morpholino group. Since variable "Het" is not defined as an O-ethylene-1-morpholino group in any of these claims, these claims are not anticipated or rendered obvious by Xiang et al.

12. Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 3/31/2009 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NOBLE JARRELL whose telephone number is (571)272-9077. The examiner can normally be reached on M-F 7:30 A.M - 6:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Noble Jarrell/
Examiner, Art Unit 1624

/James O. Wilson/
Supervisory Patent Examiner, Art Unit 1624